Applicants regard as the invention. Specifically, the Examiner asserts that the recitation of the vector "pSMT3" as its sole designation is unclear. The Applicants have amended claim 26 to include reference to SEQ ID NO: 36. Therefore, the Applicants respectfully assert that this rejection has been traversed.

Rejections under 35 U.S.C. § 102

6) The Examiner has rejected claims 11 and 17 under 35 U.S.C. § 102 (b) as being anticipated by Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754, hereinafter "Kapoor"). The Examiner asserts that Horwitz discloses vaccinating agents using Mycobacterium tuberculosis extracellular proteins and that Kapoor teaches the 12, 14 and 71 kD proteins as secreted molecules. The Applicants respectfully disagree. The Kapoor patent is entitled "Membrane associated Immunogens of Mycobacterium." The Kapoor reference neither suggests nor discloses that the 12 kD, 14 kD or 71 kD M. tuberculosis proteins are **secreted** extracellular proteins. In fact, the reference to these proteins is so sparse as to be totally non-enabling and because the Kapoor only discloses membrane bound proteins, enablement for secreted major extracrellular proteins is completely lacking. Moreover, there are numerous M. tuberculosis proteins that have molecular weights in the 12 kD, 14 kD and 71 kD range. Not all are secreted and not all are the same as those very specifically defined in the present application. A person having ordinary skill in the art could not tell specifically what proteins the Kapoor references teaches except that **Kapoor does not teach a secreted protein and his patent** specifically addresses only membrane-bound, not secreted proteins. Therefore, the only logical nexus between the 12 kD, 14 kD and 71 kD proteins disclosed and the Kapoor reference would be with membrane-bound proteins not secreted proteins.

Finally, it is axiomatic that in order for a reference to anticipate a later filed patent application, that reference must be enabling In re Donohue , 766 F.2d 531, 533 (Fed. Cir. 1985), and operative. U.S. v. Adams , 383 U.S. 39, 50 (1966). In the present case, the Examiner has cited Horwitz as evidenced by Kapoor. Horwitz enables a vaccine composition and method of inducing an immune response in an animal. The vaccine composition disclosed in Horwitz is a mixture of major extracellular (secreted) proteins derived from M. tuberculosis culture filtrates. It neither discloses or enables a vaccine

composition made form isolated, purified (individually or in combination) M. tuberculosis major extracellular proteins and/or purified immunodominant peptide subunitis. The Kapoor reference merely discloses the existence of unidentified M. tuberculosis proteins having molecular weights that include 12 kD, 14 kD and 71 kD. Kapoor does not teach how to make or use vaccine compositions using isolated, purified M. tuberculosis 12 kD, 14 kD and/or 71 kD major extracellular proteins (secreted proteins). Therefore, the Applicants respectfully assert that Horwitz as evidenced by Kapoor is a non-enabling reference and therefore, based on the Court of Appeals for the Federal Circuit's (CAFC) holding in In re Donohue and the United States Supreme Court's holding in U.S. v. Adams, do not anticipate the vaccine compositions claims in the present application and request that the Examiner withdraw her 35 U.S.C. § 102 (b) rejections as to claims 11 and 17 based on these non-enabling references.

7) The Examiner has rejected claims 11-13 and 17-19 under 35 U.S.C. § 102 (b) as being anticipated by Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130). The Examiner correctly asserts that claims 12, 18, and 11 in part and 17 in part are drawn to vaccinating agents comprising at least the M. tuberculosis 32 kD antigen and that Borremans teaches a secreted M. tuberculosis 32 kD . The Applicants has amended claims 12, 18 and 11 in part and 17 in part so that they no longer recite the 32 kD protein of M. tuberculosis. Therefore, the Applicants respectfully assert that this rejection has been traversed. The Applicants have elected to further the prosecution of embodiments including the M. tuberculosis 32 kD protein in continuing applications.

The Examiner has also correctly asserted that claims 13 and 19 are drawn to the entire M. tuberculosis 32 kD extracellular protein because the open ended language "comprising" is used in conjunction with the recitation of M. tuberculosis 32 kD immunodominant fragments and therefore would embrace the entire 32 kD antigen. The Examiner points out that Borremans teaches a secreted M. tuberculosis 32 kD. The Applicants have amended claims 13 and 19 by substituting the transitional term "consisting essentially of" for comprising. Therefore, the Applicants respectfully assert that this rejection has been traversed. The Applicants have elected to further the

prosecution of embodiments including the M. tuberculosis 32 kD protein in continuing applications.

8) The Examiner has rejected claims 13 and 19 under 35 U.S.C. § 102 (e) as being anticipated by Content et al. (US 5,916,558). Content discloses the M. tuberculosis 32 kD amino acid sequence including sequences that contain, in part SEQ ID NO 104 and SEQ ID NO 138 of the present application. Therefore, to simplify the prosecution of the present application, the Applicants have amended claims 13 and 19 so that they no longer include SEQ ID NO 104 or SEQ ID NO 138. Therefore, the Applicants respectfully assert that this rejection has been traversed. The Applicants have elected to further the prosecution of embodiments including SEQ ID NO 104 and SEQ ID NO 138. of the M. tuberculosis 32 kD protein in continuing applications.

9) The Examiner has rejected claims 11-25 under 35 U.S.C. § 102 (b) as being anticipated by Content et al. (EP 419,355 hereinafter Content EP). Content EP discloses the M. tuberculosis 32 kD amino acid sequence including sequences that contain, in part SEQ ID NO 104 and SEQ ID NO 138 of the present application. Therefore, to simplify the prosecution of the present application, the Applicants have amended claims 11, 14, 15, 17, 18, 20, 21, 23 and 24 so that the M. tuberculosis 32 kD protein is no longer claimed. Claims 16 and 22 have been amended so that they no longer include SEQ ID NO 104 or SEQ ID NO 138. Therefore, the Applicants respectfully assert that this rejection has been traversed. The Applicants have elected to further the prosecution of embodiments including the whole 32 kD protein and embodiments containing SEQ ID NO 104 and SEQ ID NO 138. of the M. tuberculosis 32 kD protein in continuing applications.

Rejections under 35 U.S.C. § 103 (a)

11) The Examiner has rejected claims 1, 4, 6 and 9 35 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Kapoor et al. (US 5,330,754) in view of either Yoshimoto et al. (US 4,789,658 hereinafter "Yoshimoto") or Roskam et al (US 5,417,970 hereinafter "Roskam") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Essentially, the Examiner has asserted that based on one or more combination of the above-cited references, it would have been pima facia obvious for a person of ordinary skill in the art

to make M. tuberculosis vaccine compositions that included either Interleukin-12 (IL-12), MF59 or both. Moreover, the Examiner asserts that having combined the M. tuberculosis secreted major extracellular proteins of the present invention with the adjuvants disclosed in either Yoshimoto and/or Roskam combined with common scientific knowledge as evidenced by Paul, that there would have been a reasonable expectation that efficacious M. tuberculosis vaccines would have resulted. The Applicants respectfully disagree.

The Applicants acknowledges that a skilled immunologist would be motivated to seek the most efficacious vaccine composition possible. Historically, immunologist have used myriad different adjuvant and adjuvant-like ingredients in order to increase vaccine potency, specificity and to target specific components of the immune responses (cellular versus humoral, for example). Therefore, the Applicants agree that it is prima facia obvious for an skilled immunologist to **try** various adjuvants. However, "obvious to try" is not the proper standard for a rejection under 35 U.S.C. § 103(a). In re O'Farrell, 7 U.S.C. § 1673 (Fed. Cir. 1988). Remarks in O'Farrell are particularly relevant here.

> "In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was 'obvious to try' was to explore new technology or general approach seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." Id. at 1681 (citations omitted).

The quotation from O'Farrell accurately depicts the situation here. The effect that an adjuvant has on vaccine efficacy is highly variable and must be carefully assessed for each immunogen-adjuvant mixture. Selection of the appropriate adjuvant and balancing the immunogen-to-adjuvant ratio is a sophisticated, highly experimental process. In the present case, as depicted in Figs. 22, 23, 24 and 25 together with the accompanying specification text at pages 125-132, including Examples 30-34, such experiments are described. The cited portions of the present specification demonstrate that success is

not assured and that more than routine experimentation is crucial to achieving the optimum immunogen-adjuvant mixture.

Moreover, the Examiner consistently relies on the Paul reference to support her assertion that is "well known in the art to use adjuvants in combination with antigens to make vaccines." However, it must be stressed that Paul is a textbook reference intended as a general teaching aid for persons seeking guidance in vaccine development. The cited sections, 1327-1328, offer only a brief description of adjuvants in the most general fashion. However, even in this limited teaching, Paul clearly suggests that not all adjuvants are appropriate for all applications. For example, at page 1327, second column lines 36-40 Paul states:

> "Though having an excellent safety record, it (Alum adjuvants) has generally proved to have a mediocre record-particularly in enhancing cell-mediated immune responses to subunit preparations, which are the basis of many current candidate vaccines."

Therefore, Paul suggests that some vaccine adjuvants will not work for all applications and, by implication, it is necessary to evaluate the performance of each adjuvant candidate with each immunogen combination before being able to determine which adjuvant(s) will be optimum. In other words, a person of ordinary skill in the art must **try** various immunogen-adjuvant combinations before hitting on the optimum combination.

Taking each of the references for individually, the Applicants will further demonstrate that each reference fails to provide teachings as to "...which parameters were critical or ... direction as to which of many possible choices is likely to be successful" as required by the CAFC in O'Farrell. Yoshimoto teaches methods for preparing IL-2 and drugs containing IL-2. Roskam teaches methods for preparing glycosylated IL-2 and drugs containing glycosylated IL-2. No mention is made of IL12 (the claimed interleukin of the present invention. Interleukins are a diverse group of cytokines and generalizations between interleukins as to efficacy for a specific application difficult, if not impossible to make. Therefore, absent some other teaching showing that IL-2 and IL-12 have identical activities, the Yoshimoto and Roskam references cannot be consider to provide sufficient teachings to satisfy the CAFC's test in O'Farrell. Moreover, even assuming IL-2 was identical in activity to IL-12, or should

the Examiner cite an IL-12 reference similar to Yoshimoto or Roskam, the same degree of non-routine experimentation would be necessary to demonstrate vaccine efficacy for IL-12 as would be required for IL-2, or any interleukin.

Neither Yoshimoto nor Roskam teach which parameters are critical in determining the optimum immunogen-to-adjuvant ratio for vaccine compositions intended to provide therapeutic and/or prophylactic protection against infectious agents. Paul teaches that adjuvants which induce a measurable humoral response may not elicit a satisfactory cell mediated immune response. Moreover, Paul does not teach how to select adjuvants that enhance one form of the immune response preferentially to another. In the present application, it is a cell medicated immune response that is primarily taught. Therefore, without further information, persons having ordinary skill in the art would understand Paul to infer that some adjuvants elicit strong humoral responses without stimulating a cellular response. Yoshimoto and Roskam do not teach what parameters are crucial in selecting an adjuvant that favors one arm of the immune system to another. In other words, Paul, Yoshimoto and Roskam offer an open invitation to **try.** Nothing more. Finally, as previously discussed, Horwitz and Kapoor do not provide guidance for preparing vaccine compositions using isolated, purified bacterial antigens and therefore and do not make up the deficiencies in Yoshimoto and Roskam. No combination of the cited references provides teachings as to which parameters are critical in determining the optimum adjuvant for stimulation the cellular immune response, nor the optimum immunogen-to-adjuvant ratio for sub-unit vaccine compositions.

In conclusion, it is well established that "obvious to try" is not the proper standard for a rejection under 35 U.S.C. § 103(a). Furthermore, the cited reference do not provide teachings that, in any combination, would satisfy the requirements of the CAFC as expressed in O'Farrell. Therefore, the Applicants respectfully requests that the Examiner withdraw her "adjuvant" related 35 U.S.C. § 103(a) rejections. Specifically, the Applicants respectfully requests the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 1,4,6 and 9.

12) The Examiner has rejected claims 1, 2, 4, 6, 7 and 9 35 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Borremans (Infection

and Immunity, 1989, Vol. 57, pp. 3123-3130) in view of either Yoshimoto et al. (US 4,789,658 hereinafter "Yoshimoto") or Roskam et al (US 5,417,970 hereinafter "Roskam") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Borrmans discloses the M. tuberculosis 32 kD extracellular protein; Therefore, because the M. tuberculosis 32 kD extracellular protein is no longer recited in the amended claims, the Applicants respectfully assert that all 35 U.S.C. § 103 rejections based on these references have been traversed and respectfully request the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 1,2,4,6,7 and 9.

13) The Examiner has rejected claims 1, 2, 4, 6, 7 and 9 35 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Content et al. (EP 419,355 herein after Content EP) in view of either Yoshimoto et al. (US 4,789,658 hereinafter "Yoshimoto") or Roskam et al (US 5,417,970 hereinafter "Roskam") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Content EP discloses peptides that include SEQ ID NO 104 and SEQ ID NO 138 of the present application which are no longer recited in the amended claims. Therefore, because SEQ ID NO 104 and SEQ ID NO 138 are no longer recited in the amended claims, the Applicants respectfully assert that all 35 U.S.C. § 103 rejections based on these references have been traversed and respectfully request the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 1,2,4,6,7 and 9.

14) The Examiner has rejected claims 1 and 6 35 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Kapoor et al. (US 5,330,754) in view of Kaslow et al (5,217,898 hereinafter "Kaslow") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Essentially, the Examiner has asserted that based on one or more combination of the above-cited references, it would have been pima facia obvious for a person of ordinary skill in the art to make M. tuberculosis vaccine compositions that included either Interleukin-12 (IL-12), MF59 or both. Moreover, the Examiner asserts that having combined the M. tuberculosis secreted major extracellular proteins of the present invention with the adjuvants disclosed in Kaslow combined with common scientific knowledge as evidenced by Paul, that there would have been a reasonable expectation

that efficacious M. tuberculosis vaccines would have resulted. For reasons similar to those stated in paragraph 11 supra, the Applicants respectfully disagree.

The Applicants acknowledges that a skilled immunologist would be motivated to seek the most efficacious vaccine composition possible. Historically, immunologist have used myriad different adjuvant and adjuvant-like ingredients in order to increase vaccine potency, specificity and to target specific components of the immune responses (cellular versus humoral, for example). Therefore, the Applicants agree that it is prima facia obvious for an skilled immunologist to **try** various adjuvants. However, "obvious to try" is not the proper standard for a rejection under 35 U.S.C. § 103(a). In re O'Farrell, 7 U.S.C. § 1673 (Fed. Cir. 1988). Remarks in O'Farrell are particularly relevant here.

> "In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was 'obvious to try' was to explore new technology or general approach seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." Id. at 1681 (citations omitted).

The quotation from O'Farrell accurately depicts the situation here. The effect that an adjuvant has on vaccine efficacy is highly variable and must be carefully assessed for each immunogen-adjuvant mixture. Selection of the appropriate adjuvant and balancing the immunogen-to-adjuvant ratio is a sophisticated, highly experimental process. In the present case, as depicted in Figs. 22, 23, 24 and 25 together with the accompanying specification text at pages 125-132, including Examples 30-34, such experiments are described. The cited portions of the present specification demonstrate that success is not assured and that more than routine experimentation is crucial to achieving the optimum immunogen-adjuvant mixture.

Moreover, the Examiner consistently relies on the Paul reference to support her assertion that is "well known in the art to use adjuvants in combination with antigens to make vaccines." However, it must be stressed that Paul is a textbook reference

intended as a general teaching aid for persons seeking guidance in vaccine development. The cited sections, 1327-1328, offer only a brief description of adjuvants in the most general fashion. However, even in this limited teaching, Paul clearly suggests that not all adjuvants are appropriate for all applications. For example, at page 1327, second column lines 36-40 Paul states:

> "Though having an excellent safety record, it (Alum adjuvants) has generally proved to have a mediocre record-particularly in enhancing cell-mediated immune responses to subunit preparations, which are the basis of many current candidate vaccines."

Therefore, Paul suggests that some vaccine adjuvants will not work for all applications and, by implication, it is necessary to evaluate the performance of each adjuvant candidate with each immunogen combination before being able to determine which adjuvant(s) will be optimum. In other words, a person of ordinary skill in the art must **try** various immunogen-adjuvant combinations before hitting on the optimum combination.

Kaslow teaches the use of MF-59 and Freunds adjuvant in combination with a recombinant Pfs25 antigen derived from Plasmodium falciparum. However, the immune response measure, optimized and taught in Kaslow is a humoral response (production of mouse monoclonal antibodies). Kaslow et al does not provide teachings as to which parameters are critical in determining the optimum immunogen-to-adjuvant ratio for vaccine compositions intended to invoke a cell mediated response against sub-unit vaccines (including isolated, purified bacterial antigens and peptides) derived from M. tuberculosis.

Paul teaches that adjuvants which induce a measurable humoral response may not elicit a satisfactory cell mediated immune response. Moreover, Paul does not teach how to select adjuvants that enhance one form of the immune response preferentially to another. In the present application, it is a cell medicated immune response that is primarily taught. Therefore, without further information, persons having ordinary skill in the art would understand Paul to infer that some adjuvants elicit strong humoral responses without stimulating a cellular response.

In other words, Paul and Kaslow offer an open invitation to **try.** Nothing more. Finally, as previously discussed, Horwitz and Kapoor do not provide guidance for

preparing vaccine compositions using isolated, purified bacterial antigens and therefore and do not make up the deficiencies in Yoshimoto and Roskam. No combination of the cited references provides teachings as to which parameters are critical in determining the optimum adjuvant for stimulation the cellular immune response, nor the optimum immunogen-to-adjuvant ratio for sub-unit vaccine compositions.

In conclusion, it is well established that "obvious to try" is not the proper standard for a rejection under 35 U.S.C. § 103(a). Furthermore, the cited reference do not provide teachings that, in any combination, would satisfy the requirements of the CAFC as expressed in O'Farrell. Therefore, the Applicants respectfully requests the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 1 and 6.

15) The Examiner has rejected claims 1 and 6 35 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130) in view of Kaslow et al (5,217,898 hereinafter "Kaslow") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Borrmans discloses the M. tuberculosis 32 kD extracellular protein; Therefore, because the M. tuberculosis 32 kD extracellular protein is no longer recited in the amended claims, the Applicants respectfully assert that all 35 U.S.C. § 103 rejections based on these references have been traversed and respectfully request the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 1 and 6.

16) The Examiner has rejected claims 1 and 6 35 under U.S.C. § 103 (a) as unpatentable over Content et al. (EP 419,355 herein after Content EP) in view of in view of Kaslow et al (5,217,898 hereinafter "Kaslow") and what is well known in the art as exemplified by the teachings in Paul (Immunology, 1993, pp 1327-1328). Content EP discloses peptides that include SEQ ID NO 104 and SEQ ID NO 138 of the present application which are no longer recited in the amended claims. Therefore, because SEQ ID NO 104 and SEQ ID NO 138 are no longer recited in the amended claims, the Applicants respectfully assert that all 35 U.S.C. § 103 (a) rejections based on these references have been traversed and respectfully request the Examiner to withdraw her 35 U.S.C. § 103 (a) rejections as to claims 1 and 6.

17) The Examiner has rejected claims 5 and 10 under U.S.C. § 103 (a) as unpatentable over Horwitz (US 5,108,745) as evidenced by Kapoor et al (US 5,330,754, hereinafter "Kapoor") or Horwitz (US 5,108,745) as evidenced by Borremans (Infection and Immunity, 1989, Vol. 57, pp. 3123-3130) or Content et al. (EP 419,355 hereinafter Content EP) in view of Kaslow et al (5,217,898 hereinafter "Kaslow") and either Yoshimoto et al. (US 4,789,658 hereinafter "Yoshimoto") or Roskam et al (US 5,417,970 hereinafter "Roskam"). First, the Applicant believes that the claims from which claims 5 and 10 depend are now patentable based on the amendments and arguments contained herein. Claims that depend from allowable independent claims are themselves allowable. Moreover, for the reasons stated above in paragraphs 11 and 14, all the cited references provide is another "invitation to try." Whether a combination of MF59 and IL-12 would be additive, synergistic, antagonistic or have no effect with the vaccine compositions of the present invention cannot be determined by supposition based on prior art. Extensive experimentation is required. In the present case the experiments were performed (see, for example Figs. 23 and 24 of the present application).

In conclusion, it is well established that "obvious to try" is not the proper standard for a rejection under 35 U.S.C. § 103 (a). Furthermore, the cited references do not provide teachings that, in any combination, would satisfy the requirements of the CAFC as expressed in O'Farrell. Therefore, the Applicants respectfully requests the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claims 5 and 10.

18) The Examiner has rejected claim 27 under U.S.C. § 103 (a) as unpatentable over Content et al. (EP 419,355 herein after Content EP) in view of in view of Bloom et al. (US 5,505,005 herein after Bloom). Taken together, Content EP and Bloom disclose the 32 kD antigen of M. tuberculosis vaccine compositions related thereto and methods for making the 32 kD using recombinant methods. The claims of the present application no longer recite the M. tuberculosis 32 kD protein. Therefore the Applicants respectfully assert that all 35 U.S.C. § 103 rejections based on these references have been traversed and respectfully request the Examiner to withdraw her 35 U.S.C. § 103(a) rejections as to claim 27.

In view of the above remarks and amendments, it is submitted that the pending claims are in condition for allowance and their allowance is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

No additional fees are seen as being necessary in connection for this amendment. However, the Examiner is authorized to charge any additional fees or credit any overpayment to Deposit Account 50-1901.

If any issues remain, the Examiner is urged to contact the undersigned by telephone for a prompt resolution thereof.

Respectfully submitted,

June 17, 2002

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Registration No. 39, 645

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1. A vaccinating agent for use in promoting an effective immune response, in a mammalian host, against an infectious pathogen from the genus Mycobacterium, said vaccinating agent comprising:

at least a portion of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof; and

an adjuvant selected from the group consisting of IL-12 and MF 59.

2. The vaccinating agent of claim 1 wherein said at least one majorly abundant extracellular product is M. tuberculosis [32A] 30 KD protein.

3. The vaccinating agent of claim 1 wherein said at least one majorly abundant extracellular product is a mixture of M. tuberculosis 32A KD protein, 30 KD protein, and 16 KD protein.

4. The vaccinating agent of claim 1 wherein said adjuvant is IL-12.

5. The vaccinating agent of claim 1 wherein said adjuvant is a mixture of IL-12 and MF 59.

6. A method for immunizing a mammalian host against an infectious pathogen of the genus Mycobacterium, said method comprising the steps of:

providing a vaccinating agent comprising at least a portion of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof, and ad adjuvant selected from the group consisting of IL-12 and MF 59; and

introducing said vaccinating agent into said mammalian host to induce an effective immune response to subsequent infection by said infectious pathogen.

7. The method of claim 6 wherein said at least one majorly abundant extracellular product is M. tuberculosis [32A] 30 KD protein.

8. The method of claim 6 wherein said at least one majorly abundant extracllular product is a mixture of M. tuberculosis 32A KD protein, 30 KD protein and 16 KD protein.

9. The method of claim 6 wherein said adjuvant is IL-12.

10. The method of claim 6 wherein said adjuvant is a mixture of IL-12 and MF 59.

11. A vaccinating agent for use in promoting an effective immune response, in a mammalian host, against an infectious pathogen from the genus Mycobacterium, said vaccinating agent comprising:

at least one immunodominant epitope of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein, and respective analogs, homologs, and subunits thereof.

12. The vaccinating agent of claim 11 wherein said at least one majorly abundant extracellular product is M. tuberculosis [32A] 30 KD protein.

13. The vaccinating agent of claim 12 wherein said at least one immunodominant epitope is selected from the group consisting of M. tuberculosis 32A KD protein subunits having the amino acid sequences

Peptide Sequence															**Seq. ID No.**
[G	L	R	A	Q	D	D	F	S	G	W	D	I	N	T	104]
W	D	I	N	T	P	A	F	E	W	Y	D	Q	S	G	106
P	A	F	E	W	Y	D	Q	S	G	L	S	V	V	M	107
P	V	G	G	Q	S	S	F	Y	S	D	W	Y	Q	P	110
G	C	Q	T	Y	K	W	E	T	F	L	T	S	E	L	114
K	W	E	T	F	L	T	S	E	L	P	G	W	L	Q	115
A	N	R	H	V	K	P	T	G	S	A	V	V	G	L	118
A	V	V	G	L	S	M	A	A	S	S	A	L	T	L	120
S	A	L	T	L	A	I	Y	H	P	Q	Q	F	V	Y	122

A	I	Y	H	P	Q	Q	F	V	Y	A	G	A	M	S	123
Q	Q	F	V	Y	A	G	A	M	S	G	L	L	D	P	124
G	L	L	D	P	S	Q	A	M	G	P	T	L	I	G	126
S	Q	A	M	G	P	T	L	I	G	L	A	M	G	D	127
N	D	P	L	L	N	V	G	K	L	I	A	N	N	T	134
N	V	G	K	L	I	A	N	N	T	R	V	W	V	Y	135
I	A	N	N	T	R	V	W	V	Y	C	G	N	G	K	136
[C	G	N	G	K	P	S	D	L	G	G	N	N	L	P	138]

and respective analogs, homologs, and subunits thereof including single or multiple amino acid substitutions, deletions, insertions, and inversions.

14. An immunodiagnositc agent for use in promoting a detectable immune response in a mammalian host identifying an infectious pathogen from the genus Mycobacterium, said immunodiagnostic agent comprising:

at least one immunodominant epitope of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof.

15. The immunodiagnostic agent of claim 14 wherein said at least one majorly abundant extracellular product is m. tuberculosis [32A] <u>30</u> KD protein.

16. The immunodiagnostic agent of claim 15 wherein said at least one immunodominant epitope is selected from the group consisting of M. tubercuolsis 32 KD protein subunits having the amino acid sequences

Peptide Sequence															**Seq. ID No.**
[G	L	R	A	Q	D	D	F	S	G	W	D	I	N	T	104]
W	D	I	N	T	P	A	F	E	W	Y	D	Q	S	G	106
P	A	F	E	W	Y	D	Q	S	G	L	S	V	V	M	107

P	V	G	G	Q	S	S	F	Y	S	D	W	Y	Q	P	110
G	C	Q	T	Y	K	W	E	T	F	L	T	S	E	L	114
K	W	E	T	F	L	T	S	E	L	P	G	W	L	Q	115
A	N	R	H	V	K	P	T	G	S	A	V	V	G	L	118
A	V	V	G	L	S	M	A	A	S	S	A	L	T	L	120
S	A	L	T	L	A	I	Y	H	P	Q	Q	F	V	Y	122
A	I	Y	H	P	Q	Q	F	V	Y	A	G	A	M	S	123
Q	Q	F	V	Y	A	G	A	M	S	G	L	L	D	P	124
G	L	L	D	P	S	Q	A	M	G	P	T	L	I	G	126
S	Q	A	M	G	P	T	L	I	G	L	A	M	G	D	127
N	D	P	L	L	N	V	G	K	L	I	A	N	N	T	134
N	V	G	K	L	I	A	N	N	T	R	V	W	V	Y	135
I	A	N	N	T	R	V	W	V	Y	C	G	N	G	K	136
[C	G	N	G	K	P	S	D	L	G	G	N	N	L	P	138]

and respective analogs, homologs, and subunits thereof including single or multiple amino acid substitutions, deletions, insertions, and inversions.

17. A method of immunizing a mammalian host against an infectious pathogen of the genus Mycobacterium, said method comprising the steps of:

providing at least one immunodominant epitope of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof; and

introducing said at least one immunodominant epitope to said mammalian host to induce an effective immune response to subsequent infection by said infectious pathogen.

18. The method of claim 17 wherein said at least one majorly abundant extracellular product is M. tuberculosis [32A] <u>30</u> KD protein.

19 The method of claim 18 wherein said at least on immunodominant epitope is selected from the group consisting of M. tuberculosis 32A KD protein subunits having the amino acid sequences

Peptide Sequence															**Seq. ID No.**
[G	L	R	A	Q	D	D	F	S	G	W	D	I	N	T	104]
W	D	I	N	T	P	A	F	E	W	Y	D	Q	S	G	106
P	A	F	E	W	Y	D	Q	S	G	L	S	V	V	M	107
P	V	G	G	Q	S	S	F	Y	S	D	W	Y	Q	P	110
G	C	Q	T	Y	K	W	E	T	F	L	T	S	E	L	114
K	W	E	T	F	L	T	S	E	L	P	G	W	L	Q	115
A	N	R	H	V	K	P	T	G	S	A	V	V	G	L	118
A	V	V	G	L	S	M	A	A	S	S	A	L	T	L	120
S	A	L	T	L	A	I	Y	H	P	Q	Q	F	V	Y	122
A	I	Y	H	P	Q	Q	F	V	Y	A	G	A	M	S	123
Q	Q	F	V	Y	A	G	A	M	S	G	L	L	D	P	124
G	L	L	D	P	S	Q	A	M	G	P	T	L	I	G	126
S	Q	A	M	G	P	T	L	I	G	L	A	M	G	D	127
N	D	P	L	L	N	V	G	K	L	I	A	N	N	T	134
N	V	G	K	L	I	A	N	N	T	R	V	W	V	Y	135
I	A	N	N	T	R	V	W	V	Y	C	G	N	G	K	136
[C	G	N	G	K	P	S	D	L	G	G	N	N	L	P	138]

and respective analogs, homolgos, and subunits thereof including single or multiple amino acid substitutions, deletions, insertions, and inversions.

20. A method for detecting the presence of an immune response in a mammal against a pathogen of the genus Mycobacterium, said method comprising the steps of:

providing at least one immunodominant epitope of at least one majorly abundant extracellular product selected from the group consisting of M. tuberculosis

110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof;

administering said at least one immunodominant epitope to said mammal; and

measuring the resultant immune response.

21. The method of claim 20 wherein said at least one majorly abundant extracellular product is M. tuberculosis [32A] 30 KD protein.

22. The method of claim 21 wherein said at least one immunodominant epitope is selected from the group consisting of M. tuberculosis 32A KD protein subunits having the amino acid sequences

Peptide Sequence															Seq. ID No.
[G	L	R	A	Q	D	D	F	S	G	W	D	I	N	T	104]
W	D	I	N	T	P	A	F	E	W	Y	D	Q	S	G	106
P	A	F	E	W	Y	D	Q	S	G	L	S	V	V	M	107
P	V	G	G	Q	S	S	F	Y	S	D	W	Y	Q	P	110
G	C	Q	T	Y	K	W	E	T	F	L	T	S	E	L	114
K	W	E	T	F	L	T	S	E	L	P	G	W	L	Q	115
A	N	R	H	V	K	P	T	G	S	A	V	V	G	L	118
A	V	V	G	L	S	M	A	A	S	S	A	L	T	L	120
S	A	L	T	L	A	I	Y	H	P	Q	Q	F	V	Y	122
A	I	Y	H	P	Q	Q	F	V	Y	A	G	A	M	S	123
Q	Q	F	V	Y	A	G	A	M	S	G	L	L	D	P	124
G	L	L	D	P	S	Q	A	M	G	P	T	L	I	G	126
S	Q	A	M	G	P	T	L	I	G	L	A	M	G	D	127

N	D	P	L	L	N	V	G	K	L	I	A	N	N	T	134
N	V	G	K	L	I	A	N	N	T	R	V	W	V	Y	135
I	A	N	N	T	R	V	W	V	Y	C	G	N	G	K	136
[C	G	N	G	K	P	S	D	L	G	G	N	N	L	P	138]

and respective analogs, homolgos, and subunits thereof including single or multiple amino acid substitutions, deletions, insertions, and inversions.

23. A process for producing a majorly abundant extracellular product selected from the group consisting of M. tuberculosis 110 KD protein, 80 KD protein, 71 KD protein, 58 KD protein, 45 KD protein, [32A KD protein, 32B KD protein,] 30 KD protein, 24 KD protein, 23.5 KD protein, 23 KD protein, 16 KD protein, 14 KD protein, 12 KD protein and respective analogs, homologs, and subunits thereof, said process comprising the steps of:

transforming a host cell with a vector to form a transformed cell, said vector comprising a nucleic acid molecule encoding one of said majorly abundant extracellular products; and

culturing said transformed cell to thereby produce said majorly abundant extracellular product.

24. The process of claim 23 wherein said nucleic acid molecule encodes for the [32A] <u>30</u> KD M. tuberculosis protein.

25. The process of claim 24 which includes the additional step of recovering said majorly abundant extracellular product that is produced by culturing of said transformed cell.

26. The process of claim 24 wherein said vector comprises pSMT3[.] <u>having a nucleic acid molecule comprising SEQ ID NO 36.</u>

27. The process of claim 24 wherein said host cell is M. smegmatis or M. vaccae.

28. The process of claim 24 wherein said transformed cell is cultured at a temperature of 28°C.